Radiation treatment for ductal carcinoma *in situ* (DCIS): is a boost to the tumor bed necessary?

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The aim of the presented study was to evaluate the long-term outcome of breast-conserving surgery and radiation for the treatment of ductal carcinoma in situ (DCIS) and the role of the radiation boost to the tumor bed. The files of 75 women with DCIS treated by breast-conserving surgery followed by definitive radiation from 1988 to 1997 were reviewed for demographic data, prognostic variables, radiation dose, radiation boost, recurrence, and outcome. Total radiation dose was 5000 cGy delivered in 25 fractions. Twenty patients (26.7%) received an additional boost to the tumor bed of 1000 cGy in 5 fractions. Median follow-up time was 81.5 months (range, 22–145). Pearson correlation coefficient and its significance was calculated between the variables. Log rank test was used to analyze differences in local recurrence rates between patients who did or did not receive a boost, and a Cox regression model was fitted to the data to predict recurrence. Ten patients (13%) had local recurrence; one patient showed lymphatic spread. Histopathologic examination revealed DCIS in 6 cases (60%) and invasive duct carcinoma in 4 (40%)(one minimally invasive). The recurrence group included 3 of the 20 patients who received a radiation boost (15%) and 7 of the 55 who did not (12.7%) (p=0.7). Correlation analysis of patient characteristics, prognostic factors, and treatment was significant only between mastitis as the presenting symptom (n=4) and longer time to recurrence (p=0.02). The recurrence rate in the present study was similar to other series of conservative treatment for DCIS of the breast. No additional value was found for the radiation boost. Larger controlled randomized studies are needed to confirm these findings.

Key words: boost, DCIS, ductal carcinoma in situ, radiation treatment

Ductal carcinoma *in situ* (DCIS) is a tumor confined to the mammary ductal system. The lesion is a precursor of invasive ductal carcinoma. About 50% of recurrences after treatment are invasive [1–3].

Before 1990, most patients with DCIS were treated by simple mastectomy, a relatively radical, albeit highly effective, approach. Later, the use of breast-conserving surgery in combination with adjuvant radiation therapy began to gain acceptance [1, 4–6]. The NSABP B-06 compared the outcome of lumpectomy, lumpectomy + radiotherapy and modified radical mastectomy in patients with early invasive breast cancer. A pathologic review revealed 76 women with DCIS, who were followed for a mean duration of 83 months. A local recurrence rate of 43% for lumpectomy alone compared with 7% for lumpectomy plus radiotherapy group and 0% for mastectomy was reported [7]. Three more recent, randomized clinical studies of the role of radiation therapy after lumpectomy in DCIS, conducted by the NSABP B-17 [1, 8], the European Organization for Research and Treatment of Cancer [4], and joint groups in the United Kingdom, Australia, and New Zealand [9], all concluded that the addition of radiotherapy reduces the rate of recurrence.

Nevertheless, the optimal choice of radiation in this procedure remains controversial, because the effect of the radiation boost is unknown. There are as yet no randomized trials that address this question.

The aim of the present study was to evaluate the long-term outcome of patients with DCIS treated with breast-conserving surgery and radiation therapy and examine the role, if any, of the radiation boost to the tumor bed.

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Patients and methods

The study sample consisted of 75 women with DCIS with or without microinvasive disease who were treated by breast-conserving surgery followed by definitive radiation between January 1, 1988 and December 31, 1997. According to our departmental policy, a boost was considered only in cases of involved/close (<0.1 cm) margins or microinvasive disease. The files were reviewed for demographic data, prognostic variables, radiation dose, radiation boost, recurrence, and outcome. Local recurrence was defined as the reappearance of the cancer in the treated breast. Median duration of follow-up was 81.5 months (range, 22–145); 91% of the population was followed for at least 5 years and 25% for more than 8 years.

Statistical analysis. Pearson correlation coefficient and its significance were calculated between the variables. Differences in local recurrence rates between patients who did and did not receive a radiation boost were analyzed by log rank test. A Cox regression model was fitted to the data to predict recurrence. A p value less than or equal to 0.05 was considered significant.

Results

Patient age ranged from 39 to 88 years (median 58). Other patients and clinical characteristics are listed in Table 1. Tumor-related features appear in Table 2. Most of the cases were detected by mammography. Fifty patients (66.6%) underwent lumpectomy and 25 (33.3%), lumpectomy with axillary lymph node dissection. Margins measured >0.1 cm in 28 patients (37%) and <0.1 cm in 35 cases (47%); in 12 cases, these data were unavailable. On histopathologic examination, all nodes were negative for metastatic disease. Twelve tumors had a microinvasive component. Re-excision of the primary tumor site was performed in 19 cases (25%). Ten patients (7.5%) received tamoxifen. The radiation dose in all cases was 5000 cGy delivered in 25 fractions by photon beam to the whole breast. Twenty patients (27%) received a boost dose to the tumor bed of 1000 cGy in 5 fractions using electron beam. The boost was administered because of uncertain clear margins in 13 patients, close margins in 5, and microinvasive disease in 2.

Ten patients (13%) had a local recurrence; one had lymphatic spread as well. Histopathologic examination revealed DCIS in 6 cases (60%) and invasive duct carcinoma in 4 (40%) (one minimally invasive). Fifty percent of the recurrences occurred around the tumor bed. Median time to recurrence was 33 months (mean, 43 months, range, 11–108).

The group with recurrence included 3 of the 20 patients who received a radiation boost (15%) and 7 of the 55 patients who did not (12.7%). This difference was not significant by log rank test (p=0.7). Pearson correlation analysis of patient characteristics, prognostic factors, and treatment (age, origin, family history, presenting symptoms, type of surgery, use of tamoxifen, etc.) yielded a significant correlation only between mastitis as a presenting symptom and longer time to recurrence (p=0.02).

Five patients developed a second malignancy. One suffered from two malignancies. The malignancies of the six patients were as follows: 3 contralateral breast carcinoma; 2 melanoma; 1 transitional cell carcinoma; 1 renal cell carcinoma.

Three patients died, all of causes unrelated to the breast cancer: one of a cerebrovascular accident, one from sepsis, and one from a myocardial infarction.

During follow-up there were no disease-related deaths in patients with noninvasive recurrence, similar to findings in

Table 1. Patients and clinical characteristics

Characteristics	Number (%)
Ethnic origin	
Ashkenazi Jew	47 (63)
Sepharadi Jew	27 (36)
Arab	1 (1.3)
Family history of breast cancer	
1st degree relative	11 (15)
2nd degree relative	2 (3)
Side affected	
Right	33 (44)
Left	42 (56)
Presenting symptoms	
Pain	2 (3)
Mastitis	4 (5)
Palpable mass	22 (29)

Table 2. Histopathology characteristics

Characteristics	No. (%)
Calcification	43 (57)
Necrosis	15 (20)
Tumor size (cm)	
Median	0.9
Range	0.01-7.5
Multifocality	12(16)
Histology	
Micropapillary	2 (3)
Cribriform	7 (9)
Solid	8 (11)
Comedo	22 (29)
Unknown	36 (48)
Microinvasive component (in addition to DCIS)	12 (16)
Margins	
>0.1 cm	28 (37)
<0.1 cm	35 (47)
Unknown	13 (17)

the literature [8, 10], or in patients with invasive recurrence At the last follow-up, all remaining patients were free of disease.

Discussion

We reviewed the files of 75 women with DCIS with or without microinvasive disease who underwent breast-sparing surgery and adjuvant radiation therapy. The local recurrence rate was 13.2% at a median follow-up of close to 7 years. This rate is in the upper range of recurrences as reported in previous studies (Tab. 3). The most important known risk factor for local recurrence is close/positive margins [19, 20]. The majority of the earlier studies limited their cases to clear margins. In our series, 47% of the patients had a clear margin width of less than 0.1cm; information on the status of surgical margins was unavailable in 16% of the patients.

It is also well recognized that the rate of breast cancer recurrence in DCIS is affected by the length of follow-up (Tab. 3) and use of tamoxifen [10]. Our follow-up time is longer than in most studies of this patient population [1, 9, 11–16]. Furthermore, most of the women in our series did not receive adjuvant tamoxifen. Since patients with a microinvasive component were included in our study, as opposed to most other studies, we investigated whether this had any influence on the rate of recurrence and found that none of the recurrences had a microinvasive component.

Radiation after surgery has proved its gain in DCIS [1, 4–6, 9, 21]. The use of a radiation boost in DCIS remains controversial (Tab. 3).

BARTELINK et al demonstrated a significant reduction in the risk of local recurrence in patients with invasive early breast cancer who underwent breast-conserving surgery and an additional radiation dose to the tumor bed [22]. No such trials have been carried out in DCIS. The lack of the gain from the radiation boost as observed in our study may be correlated with the location of the recurrence: In contrast to invasive breast cancer which usually recurs in the original tumor bed, in the present study this was true for only 50% of the recurrences. This finding may point to a different behavior of DCIS, which would also explain why the radiation boost was less effective.

In our study, the boost was restricted to patients with a microinvasive component or close surgical margins. We found no statistically significant difference in the disease-free interval between those who received the radiation therapy boost and those who did not, although ours is a relatively small sample; thus, we tentatively conclude, that the boost has no added value in this population. Nevertheless, considering that only the higher-risk patients received the extra dose of radiation therapy, we cannot exclude the possibility that by giving the boost, we "downgraded" their risk of recurrence to the level of the low-risk group (tumors with no microinvasive disease and adequate surgical margins). It is possible that the addition of a radiation boost to the low-risk patients would have yielded an even better disease-free survival. Controlled randomized studies are warranted before definitive recommendations can be made.

Table 3. DCIS: Results of treatment with conservative surgery and radiotherapy (review of the literature)

Author	No. Pts.	Years Follow-up (Median)	Rate of Recurrence (%)	% Pts. Received Boost
Kurtz et al (11) 1989	43	5.1	7	100
McCormick et al (12) 1991	54	3	18	73
Kuske et al (13) 1993	70	4	4.3	81.4
Ray et al (14) 1994	58	5.1	8.6	100
Hiramatzu et al (15) 1995	76	6.2	9.2	95
White et al (16) 1995	52	5.8	5.6	94
Fisher et al (1) 1998	411	8	12.1	*
Fisher et al (8) 2001	410	12	14.9	*
Solin et al (17) 2001	422	9.4	11	72
Joint Group (9) 2003	522	4.4	5.6	*
Sahoo et al 2005 (18) 2005	103	5.25	12.6	100
Present study	75	7.4	13	27

*A boost was not recommended

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